CLINICAL STUDIES: SKIN DISEASES IN HIV/AIDS

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National Institute of Arthritis and Musculoskeletal and Skin Diseases

Letter of Intent Receipt Date: March 15, 1995
Application Receipt Date: April 21, 1995

PURPOSE

The National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) invites applications for clinical studies on the treatment of skin diseases associated with HIV infection, including AIDS. These studies are designed primarily to evaluate innovative or new treatments and/or combination therapy in the treatment of any of the skin diseases seen in association with HIV infection, including AIDS, and compare them to more standard therapeutic approaches for these diseases, particularly in relation to efficacy, side effects and costs. It is not intended that large scale multicenter clinical trials be supported in response to this RFA, but rather that clinical studies be designed that may, once validated, form the basis for subsequent clinical trials.

HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This Request for Applications (RFA), Clinical Studies in Skin Diseases Associated with HIV/AIDS, is related to the priority area of chronic disabling conditions. Potential applicants may obtain a copy of "Healthy People 2000" (Summary Report: Stock No. 017-001-00474-0 or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the

Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic and foreign, for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government. Foreign institutions are not eligible for First Independent Research Support and Transition (FIRST) (R29) awards. Racial/ethnic minority individuals, women, and persons with disabilities are encouraged to apply as Principal Investigators.

MECHANISM OF SUPPORT

This RFA will use the National Institutes of Health (NIH) individual research project grant (R01), FIRST (R29) awards, and interactive research project grant (IRPG) mechanisms. The IRPG mechanism is described in PA-94-086, NIH Guide, Vol. 23, No. 28, July 29, 1994. Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. The total project period for applications submitted in response to the present RFA may not exceed three years. The anticipated award date is September 15, 1995. Because the nature and scope of the research proposed in response to this RFA may vary, it is anticipated that the size of an award will vary also. This RFA is a one time solicitation. Future unsolicited competing continuation applications will compete with all investigator-initiated applications and be reviewed according to the customary peer review procedures.

FUNDS AVAILABLE

The estimated funds (total costs) available for the first year of support for the entire program is anticipated to be 1.5 million dollars. The anticipated number of new awards is four to five.

RESEARCH OBJECTIVES

Background

Previously supported studies of the natural history of HIV infection, including AIDS, focusing on the incidence and prevalence of skin disease, have indicated that essentially all individuals infected with HIV manifest skin diseases at some time during their infection.

These diseases may be similar in nature to those seen in the non-HIV infected population, but are often more chronic and resistant to treatment. These diseases include, but are not limited to seborrheic dermatitis, psoriasis, verruca vulgaris, molluscum contagiosum, superficial fungal infections, folliculitis, both bacterial and of other etiologies, and pruritus. Other skin manifestations associated with HIV infection are more specific to individuals infected with HIV. Malignancies associated with HIV infection are not within the scope of this RFA. Although many of these diseases respond reasonably well to standard dermatologic therapy, many of them eventually become resistant to therapy and necessitate either combination treatment or innovative therapies (utilization of medications for non-FDA approved indications). These approaches have been anecdotally reported and discussed in clinical dermatologic circles, but there are no controlled clinical studies to determine the efficacy, side effects, or cost attendant with these approaches. As individuals with HIV live longer, it becomes even more likely that they will suffer significant skin manifestations potentially requiring the use of innovative therapeutic approaches. This RFA is designed to initiate studies that have the long term potential of indicating whether novel agents or therapeutic combinations are likely to be effective for these diseases.

Applications in response to this RFA are not expected to be for large scale multicenter clinical trials. Rather, it is expected that applications will be for clinical studies designed to develop and test protocols that have the potential for providing statistically valid information concerning efficacy, side effects and cost of innovative approaches to these diseases. These studies should have reproducible and quantifiable end points and appropriate control groups. Outcome measures or endpoints taking into account meaningful clinical improvement are preferred. Consideration should be given to the level of improvement (for example 20, 30, or 50 percent) that would be accepted as meaningful to clinicians or subjects. The validity of outcome measures or endpoints should be addressed. It is strongly recommended that applicants have or enlist individuals with clinical trial and biostatistical expertise and training in order to ensure proper design of these clinical investigations. The NIAMS strongly supports the provision of training or experience in biostatistics and clinical trials for individuals interested in careers in these disciplines within dermatology as a component of projects submitted in response to this RFA. The sample size considerations for the pilot study should be addressed. The application should include a plan for data management and analysis. A plan for data safety monitoring is strongly recommended, particularly for studies incorporating larger numbers of subjects or testing interventions with potentially significant adverse effects. It is also expected that there will be a discussion of the size of subsequent studies that would have sufficient power to prove the hypothesis once the clinical studies have demonstrated the validity of the approach to be taken. Therefore, the clinical studies supported under this RFA are expected to be of three years

duration to allow enough time for study design, development of the protocol, and field testing and evaluation. These studies are not to be designed to be definitive tests of therapeutic interventions that typically would require larger multicenter approaches and budgets well in excess of those expected in responses to this RFA.

The specific disease or diseases to be investigated, the interventions to be tested, and the control groups, are to be proposed by the applicant. These should be adequately justified by literature citations and/or clinical experience, which may be anecdotal.

INCLUSION OF WOMEN AND MINORITIES IN RESEARCH INVOLVING HUMAN SUBJECTS

It is the policy of the NIH that women and members of minority groups and their subpopulations must be included in all NIH supported biomedical and behavioral research projects involving human subjects, unless a clear and compelling rationale and justification is provided that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. This new policy results from the NIH Revitalization Act of 1993 (Section 492B of Public Law 103-43) and supersedes and strengthens the previous policies (Concerning the Inclusion of Women in Study Populations, and Concerning the Inclusion of Minorities in Study Populations), which have been in effect since 1990. The new policy contains some provisions that are substantially different from the 1990 policies.

All investigators proposing research involving human subjects should read the "NIH Guidelines For Inclusion of Women and Minorities as Subjects in Clinical Research," which have been published in the Federal Register of March 28, 1994 (FR 59 14508-14513) and reprinted in the NIH Guide for Grants and Contracts, Volume 23, Number 11, March 18, 1994.

Investigators also may obtain copies of the policy from the program staff listed under INQUIRIES. Program staff may also provide additional relevant information concerning the policy.

Applicants from institutions that have a General Clinical Research Center (GCRC) funded by the NIH National Center for Research Resources may wish to identify the GCRC as a resource for conducting the proposed research. If so, a letter of agreement from either the GCRC program director or Principal Investigator should be included with the application.

LETTER OF INTENT

Prospective applicants are asked to submit, by March 15, 1995, a letter of intent that includes a descriptive title of the proposed research, the name, address, and telephone number of the

Principal Investigator, the identities of other key personnel and participating institutions, and the number and title of the RFA in response to which the application may be submitted.

Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, the information that it contains allows NIAMS staff to estimate the potential review workload and to avoid conflict of interest in the review.

The letter of intent is to be sent to Dr. Alan N. Moshell at the address listed under INQUIRIES.

APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 9/91) is to be used in applying for these grants. These forms are available at most institutional offices of sponsored research; from the Office of Grants Information, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, MD 20892, telephone 301/435-0714; and from the program administrator listed under INQUIRIES.

The RFA label available in the PHS 398 (rev. 9/91) application form must be affixed to the bottom of the face page of the application. Failure to use this label could result in delayed processing of the application such that it may not reach the review committee in time for review. In addition, the RFA title and number must be typed on line 2a of the face page of the application form and the YES box must be marked.

Applications for the FIRST Award (R29) must include at least three sealed letters of reference attached to the face page of the original application. FIRST Award (R29) applications submitted without the required number of reference letters will be considered incomplete and will be returned without review.

Submit a signed, typewritten original of the application, including the Checklist, and three signed, photocopies, in one package to:

Division of Research Grants
National Institutes of Health
Westwood Building, Room 240
Bethesda, MD 20892**

At the time of submission, two additional copies of the application must also be sent to:

Tommy L. Broadwater, Ph.D.
Chief, Grants Review Branch
National Institute of Arthritis and Musculoskeletal and Skin Diseases
Natcher Building, Room 5AS-25U
45 Center Drive, MSC 6500
Bethesda, MD 20892-6500

Applications must be received by April 21, 1995. If an application is received after that date, it will be returned to the applicant without review. The Division of Research Grants (DRG) will not accept any application in response to this RFA that is essentially the same as one currently pending initial review, unless the applicant withdraws the pending application. The DRG will not accept any application that is essentially the same as one already reviewed.
This does not preclude the submission of substantial revisions of applications already reviewed, but such applications must include an introduction addressing the previous critique.

REVIEW CONSIDERATIONS

Upon receipt, applications will be reviewed for completeness by DRG and responsiveness by the NIAMS. Incomplete applications will be returned to the applicant without further consideration. If the application is not responsive to the RFA, NIAMS staff will contact the applicant to determine whether to return the application to the applicant or submit it for review in competition with unsolicited applications at the next review cycle.

Applications that are complete and responsive to the RFA will be evaluated for scientific and technical merit by an appropriate peer review group convened by the (ICD) in accordance with the review criteria stated below. As part of the initial merit review, a process (triage) may be used by the initial review group in which applications will be determined to be competitive or non-competitive based on their scientific merit relative to other applications received in response to the RFA. Applications judged to be competitive will be discussed and be assigned a priority score. Applications determined to be non-competitive will be withdrawn from further consideration and the Principal Investigator and the official signing for the applicant organization will be notified. The second level of review will be provided by the National Advisory ICD Council/Board.

Review criteria for this RFA are generally the same as those for unsolicited research grant applications.

o scientific, technical, or clinical significance and originality of proposed research;

o appropriateness and adequacy of the experimental approach and methodology proposed to carry out the research;

o qualifications and research experience of the Principal Investigator and staff, particularly, but not exclusively, in the area of the proposed research;

o availability of the resources necessary to perform the research;

o appropriateness of the proposed budget and duration in relation to the proposed research;

o adequacy of plans to include both genders and minorities and their subgroups as appropriate for the scientific goals of the research. Plans for the recruitment and retention of subjects will also be evaluated. The initial review group will also examine the provisions for the protection of human and animal subjects, the safety of the research environment, and conformance with the NIH Guidelines for the Inclusion of Women and Minorities as Subjects in Clinical Research.

AWARD CRITERIA

The anticipated date of award is September 15, 1995. Awards will be based upon the following criteria:

o priority score
o availability of funds
o programmatic priorities of the funding ICD

INQUIRIES

Written and telephone inquiries concerning this RFA are encouraged.
The opportunity to clarify any issues or questions from potential applicants is welcome.
Direct inquiries regarding programmatic issues to:

Alan N. Moshell, M.D.
Skin Diseases Program Director
National Institute of Arthritis and Musculoskeletal and Skin Diseases
Natcher Building, Room 5AS-25L

45 Center Drive
Bethesda, MD 20892-6500
Telephone: (301) 594-5017
FAX: (301) 480-4543
Email: moshella@ep.niams.nih.gov

Direct inquiries regarding fiscal matters to:

Mary L. Graham
Grants Management Officer
National Institute of Arthritis, Musculoskeletal and Skin Diseases
Natcher Building, Room 5AS-49A
Bethesda, MD 20892-6500
Telephone: (301) 594-3504
FAX: (301) 480-5450
Email: Grahamm@ep.niams.nih.gov

AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.361. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

The Public Health Service (PHS) strongly encourages all grant recipients to provide a smoke free workplace and promote the non-use of all tobacco products. This is consistent with the PHS mission to protect and advance the physical and mental health of the American people.

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